On diagnostic tools in coeliac disease and its complicated forms

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Summary and conclusions

Coeliac disease (CD) is a disorder of children and adults manifested by characteristic abnormalities of the small-intestinal mucosa that results from a permanent, genetically and immunologically based intolerance to ingested gluten. Clinical, serological and histological improvements commonly follow withdrawal of dietary gluten. Recent studies from Europe, North America and many other countries have shown a prevalence of 1 in 80 to 1 in 140 in the general population. In the Netherlands a prevalence of 1 in 198 has been reported.

Numerous diagnostic tools have evolved over the years to identify CD, the chameleon. The techniques have been either improved or innovated to detect the disease or its complications. The thesis acknowledges the application and the impact of several tools in this entity.

The historical developments of various tools are presented in section I. Despite the diversity of these tools, no one could prove optimal to, or substitute the gold standard based on small bowel histology for the diagnosis of CD.

The discovery and widespread use of serum antibody tests actually formed the main contributing factor to revise the diagnostic definition criteria of CD by excluding a follow-up biopsy and gluten challenge from the original list. However, the value of these simple, cheap and non-invasive assays declined when they were tested in clinical practice as

demonstrated in chapter one by showing that one of five patients with CD would have been missed if the diagnosis relied on serology only. The same chapter has defined for the first time, in a prospective manner, the performance of HLA-DQ typing; a test based on analysis of genetic risk factors in the diagnosis of CD. The low specificity, positive predictive value, and positive likelihood ratio of HLA-typing preclude its use as a first line strategy. Its strength in ruling out the disease is based on its high negative predictive value and negative likelihood ratio. The main outcome of this study presented in this chapter is that neither serum antibody tests nor HLA-DQ typing can replace endoscopy and duodenal biopsy when diagnosis of CD is suspected on clinical grounds. The role of these serological and HLA-DQ typing tests in screening asymptomatic individuals with autoimmune disease known to be associated with CD is presented in chapter two. Serum antibody tests are helpful in detecting hidden cases with CD while HLA-DQ typing is helpful in selecting individuals with increased risk for suffering from CD to be screened.

Imaging techniques can help to illustrate the details of abdominal organs in CD and are better tolerated by patients. Chapter three describes the radiographic findings of abdominal computerized tomography (CT) scan in CD, and shows that the technique is useful in discriminating between CD and (Pre) enteropathy-associated T-cell lymphoma. CT scan revealed less bowel wall thickening,

lymphadenopathy, and hyposplenism in responsive patients with CD to gluten free diet and refractory coeliac disease (RCD) type 1 than in patients with RCD type 2 and EATL. In chapter four, it has been revealed that ^{18}F-fluoro-deoxy-glucose positron emission tomography seems to be more effective than abdominal CT scan to detect EATL in patients with RCD. In conclusion, imaging techniques can be helpful to detect abnormalities that require further histological studies and have an important additional value in outlining further management lines in these patients where the correct diagnosis is so difficult to reach. The endoscopic tools that can visualize the affected small bowel in patients with CD are discussed in chapters five, six and seven. The video capsule endoscopy proved to be of value in detecting complications such as ulcerations, stenosis, and tumors in 44 patients with RCD examined by this tool. This method can further dictate the indication for a subsequent examination such as double-balloon enteroscopy with biopsy facility for histological assessment. Finally, chromoendoscopy can be employed to highlight the lesions when found during enteroscopy. Double-balloon enteroscopy is however more invasive and less tolerated by patients especially when conscious sedation is used rather than propofol or general anaesthesia in addition to required experience to perform the procedure.

The patchy distribution of villous atrophy may be responsible for false negative histological results in patients with CD. Chapter eight

demonstrates that patchy atrophy occurs only in RCD. The study is however based on limited number of subjects and will be important to verify the correctness of this important conclusion. Intraepithelial T-lymphocytes in patients with CD change their common surface receptors during their evolvement into neoplastic cells. Modern techniques such T-cell receptor gamma (TCR-γ) gene rearrangements clonality or immunophenotyping by flow cytometry are employed to identify this change in order to classify the intraepithelial T-lymphocytes. Chapter nine addresses the role of these two methods to identify selected cases of RCD that can evolve into lymphoma. This chapter reveals that immunophenotyping by flow cytometry is more reliable for this purpose than TCR-γ gene clonality analysis.

In conclusion, the family physician has now serological and HLA-DQ typing techniques to improve the screening of patients with this protean manifestations to undergo a small bowel biopsy, while the clinician, whether internist or gastroenterologist has new and relatively reliable techniques for the evaluation of RCD for complications. This thesis has shown that different techniques provide different data, which can be used on one side to establish or exclude the diagnosis of CD, and on the other side to identify complications. The more we know about the disease, the more doors will open for us to explore newer tools. It has to be emphasized however, that the indication for each tool has to be

based on individual grounds. On the whole this thesis demonstrate the value of personalized medicine in selecting new diagnostic tools.